

In the Claims:

Claims 1 – 122 (Canceled)

123. (Currently amended) A composition-of-matter comprising a partially glycoylated crystallized glucocerebrosidase molecule, wherein said crystallized glucocerebrosidase molecule is characterized by an X-ray diffraction capacity enabling generation of a set of structure coordinates defining a 3D structure of said glucocerebrosidase molecule or a portion thereof, wherein said set of structure coordinates comprises a set of structural coordinates as set forth in Table 4.

124. (Previously presented) The composition-of-matter of claim 123, wherein said set of structure coordinates defines said 3D structure to a resolution of 2.9 angstroms or higher.

126. (Previously presented) The composition-of-matter of claim 123, wherein said crystallized glucocerebrosidase molecule is characterized by unit cell dimensions of a = about 107.7 angstroms, b = about 285.2 angstroms and c = about 91.8 angstroms.

127. (Previously presented) The composition-of-matter of claim 123, wherein said crystallized glucocerebrosidase molecule is characterized by a crystal space group of C222₁.

128. (Previously presented) The composition-of-matter of claim 123, wherein said glucocerebrosidase molecule is capable of displaying normal enzymatic activity.

129. (Previously presented) The composition-of-matter of claim 123, wherein an amino acid sequence of said glucocerebrosidase molecule is set forth in SEQ ID NO: 1.

131. (Currently amended) A purified glucocerebrosidase preparation comprising a population of glucocerebrosidase molecules, wherein substantially each of said glucocerebrosidase molecules:

- (i) has an amino acid sequence at least 95 percent homologous to an amino acid sequence set forth by SEQ ID NO: 1-~~or 8~~;
- (ii) is glycosylated at asparagine 19, ~~or has an aspartic acid residue at, glycosylation residue 1~~ of said amino acid sequence; and
- (iii) is ~~independently~~ unglycosylated at one or more glycosylation residues selected from the group consisting of glycosylation residues 2, 3 and 4 of said amino acid sequence,

wherein said glucocerebrosidase is able to form pure glucocerebrosidase crystals having an X-ray diffraction capacity enabling generation of a set of structure coordinates defining a 3D structure of said glucocerebrosidase molecule, wherein said set of structure coordinates comprises a set of structural coordinates as set forth in Table 4.

133. (Previously presented) The glucocerebrosidase preparation of claim 131, wherein said glycosylation residue 2 is represented by Asn59 of SEQ ID NO: 1, 8 or 16.

134. (Previously presented) The glucocerebrosidase preparation of claim 131, wherein said glycosylation residue 3 is represented by Asn146 of SEQ ID NO: 1, 8 or 16.

135. (Previously presented) The glucocerebrosidase preparation of claim 131, wherein said glycosylation residue 4 is represented by Asn270 of SEQ ID NO: 1, 8 or 16.

136. (Previously presented) The glucocerebrosidase preparation of claim 131, wherein said population of glucocerebrosidase molecules has about the same capacity to catalyze hydrolysis of a glucocerebroside as a population of fully glycosylated glucocerebrosidase molecules having an amino acid sequence selected from the group consisting of SEQ ID NO: 1 or 8.

137. (Previously presented) The glucocerebrosidase preparation of claim 131, wherein at least one glycosylation moiety of each of at least some of said glucocerebrosidase molecules has at least one exposed mannose residue.

138. (Previously presented) The glucocerebrosidase preparation of claim 131, wherein at least some of said glucocerebrosidase molecules are capable of being internalized by a phagocyte.

139. (Previously presented) A pharmaceutical composition for treating a disease associated with glucocerebrosidase deficiency in a subject in need thereof, the pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as an active ingredient, the glucocerebrosidase preparation of claim 131.

140. (Previously presented) The pharmaceutical composition of claim 139, wherein said pharmaceutically acceptable carrier is selected so as to enable administration of the pharmaceutical composition via a route selected from the group consisting of the intravenous, topical, intranasal, transdermal, intradermal, oral, buccal, parenteral, rectal and inhalation route.

141. (Previously presented) An article of manufacture comprising packaging material and a pharmaceutical composition, the article of manufacture being identified for treatment of a disease associated with glucocerebrosidase deficiency in a subject in need thereof; the pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as an active ingredient, the glucocerebrosidase preparation of claim 131.

142. (Previously presented) A method of producing a glucocerebrosidase preparation suitable for treatment of a disease associated with glucocerebrosidase deficiency, the method comprising exposing a plurality of glucocerebrosidase molecules to conditions suitable for partial deglycosylation thereof so as to form a population of partially deglycosylated glucocerebrosidase molecules each characterized by an amino acid sequence:

- (i) glycosylated at, or having an aspartic acid residue at, glycosylation residue 1 thereof; and

- (ii) lacking glycosylation at one or more glycosylation residues thereof selected from the group consisting of glycosylation residues 2, 3 and 4, thereby producing the glucocerebrosidase preparation suitable for treatment of the disease associated with glucocerebrosidase deficiency.

143. (Previously presented) The method of claim 142, further comprising, prior to and/or concomitantly with said exposing said plurality of glucocerebrosidase molecules to said conditions, subjecting said plurality of glucocerebrosidase molecules to conditions suitable for exposing at least one mannose residue of at least one glycosylation moiety of each of at least some of said glucocerebrosidase molecules of said plurality of glucocerebrosidase molecules.

144. (Previously presented) The method of claim 142, further comprising subjecting said population of partially deglycosylated glucocerebrosidase molecules to conditions suitable for exposing at least one mannose residue of at least one glycosylation moiety of each at least some of said partially glycosylated glucocerebrosidase molecules.

145. (Previously presented) The method of claim 142, wherein said conditions suitable for partial deglycosylation of said glucocerebrosidase molecules include treating said plurality of glucocerebrosidase molecules with a glycosidase.

146. (Previously presented) The method of claim 142, wherein said conditions suitable for partial deglycosylation of said glucocerebrosidase molecules include treating said plurality of glucocerebrosidase molecules with peptide N-glycosidase F.

147. (Previously presented) The method of claim 142, wherein said amino acid sequence is at least 95 percent homologous to an amino acid sequence set forth by SEQ ID NO: 1 or 8;

148. (Previously presented) The method of claim 147, wherein said glycosylation residue 1 is represented by Asn19 of SEQ ID NO: 1, 8 or 16.

149. (Previously presented) The method of claim 147, wherein said glycosylation residue 2 is represented by Asn59 of SEQ ID NO: 1, 8 or 16.

150. (Previously presented) The method of claim 147, wherein said glycosylation residue 3 is represented by Asn146 of SEQ ID NO: 1, 8 or 16.

151. (Previously presented) The method of claim 147, wherein said glycosylation residue 4 is represented by Asn270 of SEQ ID NO: 1, 8 or 16.

152. (Previously presented) The method of claim 142, wherein the disease associated with glucocerebrosidase deficiency is Gaucher disease.

153. (Previously presented) A method of increasing glucocerebrosidase activity in a cell, the method comprising exposing the cell to the glucocerebrosidase preparation of claim 131, thereby inducing substantial glucocerebrosidase activity in a cell.

154. (Previously presented) A method of treating a disease associated with glucocerebrosidase deficiency in a subject in need thereof, the method comprising administering to the subject in need thereof a therapeutically effective amount of the glucocerebrosidase preparation of claim 131, thereby treating the disease associated with glucocerebrosidase deficiency in the subject.

155. (Previously presented) The method of claim 154, wherein the disease associated with glucocerebrosidase deficiency is Gaucher disease.

156. (Previously presented) A method of identifying a compound capable of correcting an impaired enzymatic activity of a mutant glucocerebrosidase molecule, the method comprising:

- (a) obtaining a first set of structure coordinates, said first set of structure coordinates defining a 3D structure of a glucocerebrosidase molecule capable of displaying normal enzymatic activity or a portion thereof;
- (b) computationally generating using said first set of structure coordinates a second set of structure coordinates, said second set of structure

coordinates defining a predicted 3D structure of the mutant glucocerebrosidase molecule or a portion thereof; and

- (c) computationally identifying, using said second set of structure coordinates, a compound capable of interacting with the mutant glucocerebrosidase molecule in such a way as to correct the impaired enzymatic activity thereof, thereby identifying the compound capable of correcting the impaired enzymatic activity of the mutant glucocerebrosidase molecule.

157. (Previously presented) A computing platform capable of generating a model representing a 3D structure of a glucocerebrosidase molecule or a portion thereof, the computing platform comprising:

- (a) a data-storage device storing data comprising a set of structure coordinates defining the 3D structure of the glucocerebrosidase molecule or the portion thereof; and
- (b) a processing unit being for generating the model representing the 3D structure from said data stored in said data-storage device.

158. (Previously presented) A computer-readable medium comprising, in a retrievable format, data including a set of structure coordinates defining a 3D structure of a glucocerebrosidase molecule or a portion thereof, wherein said set of structure coordinates defines said 3D structure at a resolution of 2.9 angstroms or higher, and/or wherein an amino acid sequence of said glucocerebrosidase molecule is partially glycosylated.

159. (Previously presented) A computer generated model representing a 3D structure of a glucocerebrosidase molecule or a portion thereof, wherein the model represents said glucocerebrosidase molecule or a portion thereof at a resolution of 2.9 angstroms or higher, and/or wherein an amino acid sequence of said glucocerebrosidase molecule is partially glycosylated.